

## PATENT COOPERATION TREATY

PCT

**NOTIFICATION OF ELECTION**  
(PCT Rule 61.2)

#### From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 12 April 2000 (12.04.00)	in its capacity as elected Office
<b>International application No.</b> PCT/US99/18961	<b>Applicant's or agent's file reference</b> 3797.35WOU2
<b>International filing date</b> (day/month/year) 19 August 1999 (19.08.99)	<b>Priority date</b> (day/month/year) 19 August 1998 (19.08.98)
<b>Applicant</b>	
HOCK, Janet, M.	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

16 March 2000 (16.03.00)

in a notice effecting later election filed with the International Bureau on:

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p><b>The International Bureau of WIPO</b>  <b>34, chemin des Colombettes</b>  <b>1211 Geneva 20, Switzerland</b></p>	<p><b>Authorized officer</b>  <b>Juan Cruz</b></p>
<p>Facsimile No.: (41-22) 740.14.35</p>	<p>Telephone No.: (41-22) 338.83.38</p>

## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

16

## (PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3797.35WOU2	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/18961	International filing date (day/month/year) 19/08/1999	Priority date (day/month/year) 19/08/1998
International Patent Classification (IPC) or national classification and IPC A61K38/29		
Applicant ELI LILLI AND COMPANY et al.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 4 sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand 16/03/2000	Date of completion of this report 02.08.2000
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 eprmu d Fax: +49 89 2399 - 4465	Authorized officer  Fayos, C Telephone No. +49 89 2399 2180



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/18961

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-4,6-46,48-53	as originally filed
5,47	with telefax of
	11/05/2000

**Claims, No.:**

1-8	filed during a personal consultation on	20/07/2000
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**Drawings, sheets:**

1/10-10/10	as originally filed
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2. The amendments have resulted in the cancellation of:

the description,      pages:  
 the claims,      Nos.:  
 the drawings,      sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.  
 claims Nos. 1-5 (industrial applicability).

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/18961

because:

the said international application, or the said claims Nos. 1-5 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. .

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims 1-5 and 7-8
	No:	Claims 6
Inventive step (IS)	Yes:	Claims 1-5 and 7-8
	No:	Claims -
Industrial applicability (IA)	Yes:	Claims 6-8; 1-5 (see separate sheet)
	No:	Claims

### 2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/18961

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

- 1- Claims 1-5 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- 2- Reference is made to the following documents:

D1: R. LINSAY ET AL.: 'RANDOMISED CONTROLLED STUDY OF EFFECT OF PARATHYROID HORMONE ON VERTEBRAL-BONE MASS AND FRACTURE INCIDENCE AMONG POSTMENOPAUSAL WOMEN ON OESTROGEN WITH OSTEOPOROSIS.' THE LANCET, vol. 350, 23 August 1997 (1997-08-23), pages 550-555, XP002127205 LONDON, GB

D2: PATENT ABSTRACTS OF JAPAN vol. 1996, no. 07, 31 July 1996 (1996-07-31) & JP 08 073376 A (ASAHI CHEM IND CO LTD), 19 March 1996 (1996-03-19)

D2A: English translation of JP 08 073376 A (ASAHI CHEM IND CO LTD), 19 March 1996 (1996-03-19)

**NOVELTY - Art. 33 (1) and (2) PCT**

- 3- **Claim 6 is not new for the following reasons:**

- 3.1- The use of hPTH(1-34) in medicine is known from e. g. D1, D2 and D2A. This implies the existence of a product (e. g. a pharmaceutical composition) comprising hPTH(1-34).

The subject matter of claim 6 refers to an article of manufacture (i. e. a product) comprising: (i) hPTH (1-34), (ii) a packaging material and (iii) a printed matter. Since the features: (ii) a packaging material and (iii) a printed matter do not constitute technical features which would differentiate a product from other ones, claim 6 is not new.

**4- Claims 1-5 and 7-8 appear to be new in the light of the prior art cited in the search report.**

4.1- None of the prior art documents cited in the search report discloses the use of hPTH (1-34) for the manufacture of a medicament for concurrently reducing the risk of both vertebral and non-vertebral bone fracture in a human subject at risk of or having osteoporosis, wherein said medicament is administered to said subject without concurrent administration of an antiresorptive agent other than vitamin D or calcium, in a daily dose of 20 µg or 40 µg for at least about 12 months up to 3 years.

Hence, claims 1-5 and 7-8 can be considered as being new.

**INVENTIVE STEP - Art. 33 (1) and (3) PCT**

5- As acknowledged in the present application (p 2 § 2), it is known that PTH increases whole bone mass, but it is commonly believed that PTH administration in humans has a negative effect on cortical bone (reduction of cortical bone mass and strength). With this respect, see e. g. D1 (p 551 c 1 § 3) which reports that: although PTH may increase cancellous bone mass, this increase might be accompanied by net loss of cortical bone, thus suggesting that PTH should decrease vertebral fracture risk but might increase peripheral bone fracture (i. e. non vertebral bone fracture).

5.1- The problem posed in the present application is to provide means for reducing the risk of **both vertebral and non-vertebral** bone fracture in a human subject at risk of or having osteoporosis.

5.2- The solution proposed in the present application is the administration of hPTH(1-34)

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/18961

without concurrent administration of an antiresorptive agent other than vitamin D or calcium, in a daily dose of 20 µg or 40 µg for at least about 12 months up to 3 years.

5.3- The closest prior art D2A discloses the intermittent administration of hPTH(1-34) without concurrent administration of an antiresorptive agent, in a dose of 100-200 units for prolonged use.

**6- Claims 1-5 and 7-8 involve an inventive step in the light of the prior art cited in the search report.**

6.1- D2A shows that the intermittent administration of hPTH(1-34) without concurrent administration of an antiresorptive agent, in a dose of 100-200 units for up to 6 months has therapeutic effects on osteoporosis without reducing cortical bone (D2A last §).

6.3- Nothing in D2A suggests that, contrary to the prejudice that hPTH(1-34) would increase non-vertebral fracture risk (see item 5- above), hPTH(1-34), without concurrent administration of an antiresorptive agent other than vitamin D or calcium, in a daily dose of 20 µg or 40 µg for at least about 12 months up to 3 years would even reduce the risk of non-vertebral bone fracture in a human subject at risk of or having osteoporosis. [This effect is supported by the technical data of the application]

6.4- Therefore, claims 1-5 and 7-8 involve an inventive step.

**INDUSTRIAL APPLICABILITY - Art. 33 (1) and (4) PCT**

**7- Claims 6-8 appear to be industrially applicable.**

8- For the assessment of the present claims 1-5 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US99/18961

known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

62  
**PATENT COOPERATION TREATY****PCT****INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>3797.35W0U2</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/18961</b>	International filing date (day/month/year) <b>19/08/1999</b>	(Earliest) Priority Date (day/month/year) <b>19/08/1998</b>
Applicant <b>ELI LILLI AND COMPANY et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

**METHOD OF INCREASING BONE TOUGHNESS AND STIFFNESS AND REDUCING FRACTURES**

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure N .

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/18961

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
**Remark:** Although claims 1-48 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark in Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/29 // (A61K38/29, 33:06), (A61K38/29, 31:59)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>R. LINSAY ET AL.: "RANDOMISED CONTROLLED STUDY OF EFFECT OF PARATHYROID HORMONE ON VERTEBRAL-BONE MASS AND FRACTURE INCIDENCE AMONG POSTMENOPAUSAL WOMEN ON OESTROGEN WITH OSTEOPOROSIS."  <b>THE LANCET</b>,  vol. 350, 23 August 1997 (1997-08-23),  pages 550-555, XP002127205  LONDON, GB  page 555, left-hand column, paragraph 4</p> <p style="text-align: center;">—/—</p>	1-59

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the International search

Date of mailing of the International search report

11 January 2000

24/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Ryckebosch, A

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	C.P. JEROME ET AL.: "EFFECT OF TREATMENT FOR 3 MONTHS WITH HUMAN PARATHYROID HORMONE 1-34 PEPTIDE IN OVARIECTOMIZED CYNOMONGOLUS MONKEYS (MACACA FASCICULARIS)." BONE, vol. 17, no. 4 SUPPL., October 1995 (1995-10), pages 415S-420S, XP000857980 NEW YORK, US page 415S, paragraphs 2,3 -page 416S, paragraphs 1,2 page 418S, paragraphs 3,4 -page 419S, paragraphs 1-3	1-59
X	PATENT ABSTRACTS OF JAPAN vol. 1996, no. 07, 31 July 1996 (1996-07-31) & JP 08 073376 A (ASAHI CHEM IND CO LTD), 19 March 1996 (1996-03-19) abstract	1-59
X	DATABASE WPI Section Ch, Week 199706 Derwent Publications Ltd., London, GB; Class B04, AN 1997-061733 XP002127206 & JP 08 310965 A (CHUGAI PHARM CO LTD), 26 November 1996 (1996-11-26) abstract	1-59
X	C. EJERSTED ET AL.: "HUMAN PARATHYROID HORMONE (1-34) AND (1-84) INCREASE THE MECHANICAL STRENGHT AND THICKNESS OF CORTICAL BONE IN RATS." JOURNAL OF BONE AND MINERAL RESEARCH, vol. 8, no. 9, September 1993 (1993-09), pages 1097-1101, XP000857986 NEW YORK, US page 1100, right-hand column, paragraph 3 -page 1101, left-hand column, paragraph 1	1-59
X	WO 98 14478 A (BETH ISRAEL DEACONESS MEDICAL CENTER) 9 April 1998 (1998-04-09) page 3, line 4 - line 28; claims; examples 4,5 page 6, line 18 - line 32	1-59
P, X	WO 99 12561 A (F. HOFFMAN-LA ROCHE AG) 18 March 1999 (1999-03-18) page 2, line 20 - line 28; claims; examples page 12, line 28 -page 13, line 23	1-59
		-/-

## INTERNATIONAL SEARCH

national Application No  
PCT/US 99/18961

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>T. HIRANO ET AL.: "ANABOLIC EFFECTS OF HUMAN BIOSYNTHETIC PARATHYROID HORMONE FRAGMENT (1-34), LY333334, ON REMODELING AND MECHANICAL PROPERTIES OF CORTICAL BONE IN RABBITS." JOURNAL OF BONE AND MINERAL RESEARCH, vol. 14, no. 4, April 1999 (1999-04), pages 536-545, XP000857985 NEW YORK, US the whole document</p> <p>-----</p>	1-59

## INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT/US 99/18961

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 08073376 A	19-03-1996	NONE	
JP 8310965 A	26-11-1996	NONE	
WO 9814478 A	09-04-1998	US 5747456 A AU 4501697 A	05-05-1998 24-04-1998
WO 9912561 A	18-03-1999	AU 9740698 A	29-03-1999



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : <b>A61K 38/29 // (A61K 38/29, 33:06) (A61K 38/29, 31:59)</b>		A1	(11) International Publication Number: <b>WO 00/10596</b>  (11) International Publication Number: <b>PCT/US99/18961</b>  (11) International Publication Number: <b>WO 00/10596</b>	(43) International Publication Date: 2 March 2000 (02.03.00)
<p>(21) International Application Number: <b>PCT/US99/18961</b></p> <p>(22) International Filing Date: 19 August 1999 (19.08.99)</p> <p>(30) Priority Data:            60/097,151 19 August 1998 (19.08.98) US            60/099,746 10 September 1998 (10.09.98) US         </p> <p>(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications            US 60/097,151 (CON)            Filed on 19 August 1998 (19.08.98)            US 60/099,746 (CON)            Filed on 10 September 1998 (10.09.98)         </p> <p>(71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).</p> <p>(72) Inventor; and            (75) Inventor/Applicant (for US only): HOCK, Janet, M. [US/US]; 7702 Candlewood Lane, Indianapolis, IN 46250 (US).</p>		<p>(74) Agent: DAIGNAULT, Ronald, A.; Merchant &amp; Gould PC, 3100 Norwest Center, 90 South Seventh Street, Minneapolis, MN 55402-4131 (US).</p> <p>(81) Designated States: AE, AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b>  <i>With international search report.</i>  <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> </p> <p>(54) Title: METHOD OF INCREASING BONE TOUGHNESS AND STIFFNESS AND REDUCING FRACTURES</p> <p>(57) Abstract</p> <p>The invention relates to a method for increasing the toughness and/or stiffness of bone and/or reducing the likelihood and/or severity of bone fracture by administering a parathyroid hormone. The method can be employed to increase toughness or stiffness of bone at a site of a potential or actual trauma, such as the hip or spine of a person at risk of or suffering from osteoporosis. The method of the invention can reduce the incidence of vertebral fracture, reduce the incidence of multiple vertebral fractures, reduce the severity of vertebral fracture, and/or reduce the incidence of non-vertebral fracture.</p>		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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DK	Denmark	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

Inte onal Application No  
PCT/US 99/18961

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K38/29 // (A61K38/29, 33:06), (A61K38/29, 31:59)

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>R. LINSAY ET AL.: "RANDOMISED CONTROLLED STUDY OF EFFECT OF PARATHYROID HORMONE ON VERTEBRAL-BONE MASS AND FRACTURE INCIDENCE AMONG POSTMENOPAUSAL WOMEN ON OESTROGEN WITH OSTEOPOROSIS."          THE LANCET,          vol. 350, 23 August 1997 (1997-08-23),          pages 550-555, XP002127205          LONDON, GB          page 555, left-hand column, paragraph 4          ----          -/-</p>	1-59

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance  
 "E" earlier document but published on or after the international filing date  
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 "O" document referring to an oral disclosure, use, exhibition or other means  
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
 "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  
 "&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 January 2000	24/01/2000
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel: (+31-70) 340-2040. Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Ryckebosch, A

# INTERNATIONAL SEARCH REPORT

Inte. onal Application No  
PCT/US 99/18961

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	C.P. JEROME ET AL.: "EFFECT OF TREATMENT FOR 3 MONTHS WITH HUMAN PARATHYROID HORMONE 1-34 PEPTIDE IN OVARIECTOMIZED CYNOMONGOLUS MONKEYS (MACACA FASCICULARIS)." BONE, vol. 17, no. 4 SUPPL., October 1995 (1995-10), pages 415S-420S, XP000857980 NEW YORK, US page 415S, paragraphs 2,3 -page 416S, paragraphs 1,2 page 418S, paragraphs 3,4 -page 419S, paragraphs 1-3 ---	1-59
X	PATENT ABSTRACTS OF JAPAN vol. 1996, no. 07, 31 July 1996 (1996-07-31) & JP 08 073376 A (ASAHI CHEM IND CO LTD), 19 March 1996 (1996-03-19) abstract ---	1-59
X	DATABASE WPI Section Ch, Week 199706 Derwent Publications Ltd., London, GB; Class B04, AN 1997-061733 XP002127206 & JP 08 310965 A (CHUGAI PHARM CO LTD), 26 November 1996 (1996-11-26) abstract ---	1-59
X	C. EJERSTED ET AL.: "HUMAN PARATHYROID HORMONE (1-34) AND (1-84) INCREASE THE MECHANICAL STRENGHT AND THICKNESS OF CORTICAL BONE IN RATS." JOURNAL OF BONE AND MINERAL RESEARCH, vol. 8, no. 9, September 1993 (1993-09), pages 1097-1101, XP000857986 NEW YORK, US page 1100, right-hand column, paragraph 3 -page 1101, left-hand column, paragraph 1 ---	1-59
X	WO 98 14478 A (BETH ISRAEL DEACONESS MEDICAL CENTER) 9 April 1998 (1998-04-09) page 3, line 4 - line 28; claims; examples 4,5 page 6, line 18 - line 32 ---	1-59
P,X	WO 99 12561 A (F. HOFFMAN-LA ROCHE AG) 18 March 1999 (1999-03-18) page 2, line 20 - line 28; claims; examples page 12, line 28 -page 13, line 23 ---	1-59
	-/-	

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/18961

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	T. HIRANO ET AL.: "ANABOLIC EFFECTS OF HUMAN BIOSYNTHETIC PARATHYROID HORMONE FRAGMENT (1-34), LY333334, ON REMODELING AND MECHANICAL PROPERTIES OF CORTICAL BONE IN RABBITS." JOURNAL OF BONE AND MINERAL RESEARCH, vol. 14, no. 4, April 1999 (1999-04), pages 536-545, XP000857985 NEW YORK, US the whole document -----	1-59

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/18961

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 1-48 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2.  Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3.  Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 99/18961

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
JP 08073376	A 19-03-1996	NONE		
JP 8310965	A 26-11-1996	NONE		
WO 9814478	A 09-04-1998	US 5747456 A		05-05-1998
		AU 4501697 A		24-04-1998
WO 9912561	A 18-03-1999	AU 9740698 A		29-03-1999